

Claims

1. A method of predicting the prognosis of a biological condition in animal tissue,
5 comprising collecting a sample comprising cells from the tissue and/or expression products from the cells,

determining an expression level of at least one gene in the sample, said gene being selected from the group of genes consisting of gene No. 1 to gene No. 562,
10 correlating the expression level to at least one standard expression level to predict the prognosis of the biological condition in the animal tissue.
2. The method of claim 1, wherein the animal tissue is selected from body organs.
15
3. The method of claim 2, wherein the animal tissue is selected from epithelial tissue in body organs.
4. The method of claim 3, wherein the animal tissue is selected from epithelial tissue in the
20 urinary bladder.
5. The method according to claim 4, wherein the stage is selected from bladder cancer stages Ta, Carcinoma in situ (CIS), T1, T2, T3 and T4.
- 25 6. The method according to claim 5, comprising determining at least the expression of a Ta stage gene from a Ta stage gene group, at least one T1 stage gene from a T1 stage gene group, at least a T2 stage gene from a T2 stage gene group, at least a T3 stage gene from a T3 stage gene group, at least a T4 stage gene group from a T4 stage gene group, wherein at least one gene from each gene group is expressed in a significantly
30 different amount in that stage than in one of the other stages.
7. The method according to claim 4, 5 or 6, wherein the stage is bladder cancer stage Ta.
8. The method according to claim 4, wherein the animal tissue is mucosa.
35
9. The method of any of the preceding claims, wherein the biological condition is an adenocarcinoma, a carcinoma, a teratoma, a sarcoma, and/or a lymphoma and/or carcinoma-in-situ, and/or dysplasia-in-situ.

10. The method of any of the preceding claims, wherein the sample is a biopsy of the tissue or of metastasis originating from said tissue.
- 5 11. The method according to any of the preceding claim 1-6, wherein the sample is a cell suspension made from the tissue.
12. The method according to any of the preceding claims, wherein the sample comprises substantially only cells from said tissue.
- 10 13. The method according to claim 9, wherein the sample comprises substantially only cells from mucosa or tumors derived from said mucosa cells.
14. The method according to any of the preceding claims, wherein the gene from the group of genes is selected individually from gene No. 1 to gene No. 188 (stages).
- 15 15. The method according to any of the preceding claims 1-13, wherein the gene from the group of genes is selected individually from gene No. 189 to gene No. 214 (recurrence).
16. The method according to any of the preceding claims 1-13, wherein the gene from the group of genes is selected individually from gene No. 215 to gene No. 232 (SCC).
- 20 17. The method according to any of the preceding claims 1-13, wherein the gene from the group of genes is selected individually from gene No. 233 to gene No. 446 (progression).
18. The method according to any of the preceding claims 1-13, wherein the gene from the group of genes is selected individually from gene No. 447 to gene No. 562 (CIS).
- 25 19. The method according to any of the preceding claims, wherein the expression level of at least two genes from the group of genes are determined.
- 30 20. The method according to any of the preceding claims, wherein the expression level of at least three genes from the group of genes are determined.
21. The method according to any of the preceding claims, wherein the expression level of at least four genes from the group of genes are determined.
- 35 22. The method according to any of the preceding claims, wherein the expression level of at least five genes from the group of genes are determined.

23. The method according to any of the preceding claims, wherein the expression level of more than six genes from the group of genes are determined.
- 5 24. The method according to any of the preceding claims, wherein the difference in expression level of a gene from the gene group to the at least one standard expression level is at least two-fold.
- 10 25. The method according to any of the preceding claims, wherein the difference in expression level of a gene from the gene group to the at least one standard expression is at least three-fold.
- 15 26. The method according to any of the preceding claims, wherein the difference in expression level of a gene from the gene group to the at least one standard expression is at least four-fold.
- 20 27. The method according to any of the preceding claims, wherein the expression level is determined by determining the mRNA of the cells.
- 25 28. The method according to any of the claims 1-26, wherein the expression level is determined by determining expression products, such as peptides, in the cells.
- 30 29. The method according to claim 28, wherein the expression level is determined by determining expression products, such as peptides, in the body fluids, such as blood, serum, plasma, faeces, mucus, sputum, cerebrospinal fluid, and/or urine.
- 35 30. The method according to any of the preceding claims, wherein the stage of the biological condition has been determined prior to the prediction of the prognosis.
31. The method according to claim 30, wherein the stage of the biological condition has been determined by histological examination of the tissue or by genotyping of the tissue.
32. The method according to claim 28 or 29, wherein the stage of the biological condition has been determined by genotyping of the tissue.
33. The method according to claim 31 or 32, wherein the stage of the biological condition has been determined by
- determining the expression of at least a first stage gene from a first stage gene group and/or at least a second stage gene from a second stage gene group, wherein at least

one of said genes is expressed in said first stage of the condition in a higher amount than in said second stage, and the other gene is expressed in said first stage of the condition in a lower amount than in said second stage of the condition,

5 correlating the expression level of the assessed genes to a standard level of expression determining the stage of the condition.

34. The method according to any of the preceding claims, wherein the expression level of at least two genes is determined, by

10

determining a first expression level of at least one gene from a first gene group, wherein the gene from the first gene group is selected from the group of gene No. 237, 238, 239, 240, 241, 242, 243, 245, 246, 247, 248, 250, 253, 254, 257, 258, 260, 263, 264, 265, 267, 270, 271, 272, 278, 283, 284, 287, 288, 290, 291, 292, 294, 297, 15 298, 300, 302, 303, 305, 309, 310, 315, 316, 317, 318, 319, 321, 324, 329, 335, 336, 337, 339, 340, 344, 346, 347, 354, 356, 358, 359, 362, 364, 365, 368, 369, 371, 372, 377, 378, 379, 380, 381, 382, 383, 384, 388, 391, 393, 395, 396, 397, 399, 402, 403, 404, 409, 413, 417, 419, 420, 421, 422, 423, 425, 427, 429, 430, 431, 432, 437, 444 (progressorgener), and

20

determining a second expression level of at least one gene from a second gene group, wherein the second gene group is selected from the group of genes No. 233, 234, 235, 236, 244, 249, 251, 252, 255, 256, 259, 261, 262, 266, 268, 269, 273, 274, 275, 276, 277, 279, 280, 281, 282, 285, 286, 289, 293, 295, 296, 299, 301, 304, 306, 25 307, 308, 311, 312, 313, 314, 320, 322, 323, 325, 326, 327, 328, 330, 331, 332, 333, 334, 338, 341, 342, 343, 345, 348, 349, 350, 351, 352, 353, 355, 357, 360, 361, 363, 366, 367, 370, 373, 374, 375, 376, 385, 386, 387, 389, 390, 392, 394, 398, 400, 401, 405, 406, 407, 408, 410, 411, 412, 414, 415, 416, 418, 424, 426, 428, 433, 434, 435, 436, 438, 439, 440, 441, 442, 443, 445, 446 (non-progressorgener), and

30

correlating the first expression level to a standard expression level for progressors, and/or the second expression level to a standard expression level for non-progressors to predict the prognosis of the biological condition in the animal tissue.

35

35. A method of determining the stage of a biological condition in animal tissue, comprising collecting a sample comprising cells from the tissue,

determining an expression level of at least one gene selected from the group of genes consisting of geneNo 1 to gene No. 562

5 correlating the expression level of the assessed genes to at least one standard level of expression determining the stage of the condition.

36. The method according to claim 36, wherein the expression level of at least two genes is determined by

10 determining the expression of at least a first stage gene from a first stage gene group and at least a second stage gene from a second stage gene group, wherein at least one of said genes is expressed in said first stage of the condition in a higher amount than in said second stage, and the other gene is expressed in said first stage of the condition
15 in a lower amount than in said second stage of the condition, and

correlating the expression level of the assessed genes to a standard level of expression determining the stage of the condition

20 37. The method according to claim 35 or 36, wherein the stage is selected from bladder cancer stages Ta, carcinoma in situ (CIS), T1, T2, T3 and T4.

38. The method according to claim 37, comprising determining at least the expression of a Ta stage gene from a Ta stage gene group, at least one T1 stage gene from a T1 stage
25 gene group, at least a T2 stage gene from a T2 stage gene group, at least a T3 stage gene from a T3 stage gene group, at least a T4 stage gene group from a T4 stage gene group, wherein at least one gene from each gene group is expressed in a significantly different amount in that stage than in one of the other stages.

30 39. The method according to claim 38, wherein a Ta stage gene is selected individually from the group of Table B1.

40. The method according to claim 38, wherein a T1 stage gene is selected individually from the group of Table B2.

35 41. The method according to claim 38, wherein a T2 stage gene is selected individually from the group of Table B3.

42. The method according to any of claims 35-41, said method comprising one or more of the features defined in any of the claims 1-34.
43. A method of determining an expression pattern of a bladder cell sample, comprising:
- 5 collecting sample comprising bladder cells and/or expression products from bladder cells,
- 10 determining the expression level of at least one gene in the sample, said gene being selected from the group of genes consisting of gene No. 1 to gene No. 562, and obtaining an expression pattern of the bladder cell sample.
44. The method according to claim 43, wherein the expression level of at least two genes are determined.
- 15 45. The method according to claim 43, wherein the expression level of at least three genes are determined.
- 20 46. The method according to claim 43, wherein the expression level of at least four genes are determined.
47. The method according to claim 43, wherein the expression level of at least five genes are determined.
- 25 48. The method according to claim 43, wherein the expression level of more than six genes are determined.
- 30 49. The method of claims 43-48, wherein the genes exclude genes which are expressed in the submucosal, muscle, or connective tissue, whereby a pattern of expression is formed for the sample which is independent of the proportion of submucosal, muscle, or connective tissue cells in the sample.
- 35 50. The method of claim 49, comprising determining the expression level of one or more genes in the sample comprising predominantly submucosal, muscle, and connective tissue cells, obtaining a second pattern, subtracting said second pattern from the expression pattern of the bladder cell sample, forming a third pattern of expression, said third pattern of expression reflecting expression of the bladder mucosa or bladder cancer cells independent of the proportion of submucosal, muscle, and connective tissue cells present in the sample.

51. The method of any of the preceding claims 43-50, wherein the sample is a biopsy of the tissue.
- 5 52. The method according to any of the preceding claim 43-51, wherein the sample is a cell suspension.
53. The method according to any of the preceding claims 43-52, wherein the sample comprises substantially only cells from said tissue.
- 10 54. The method according to claim 53, wherein the sample comprises substantially only cells from mucosa.
- 15 55. A method of predicting the prognosis a biological condition in human bladder tissue comprising,
- collecting a sample comprising cells from the tissue,
- determining an expression pattern of the cells as defined in any of claims 43-54,
- 20 correlating the determined expression pattern to a reference pattern,
- predicting the prognosis of the biological condition of said tissue.
- 25 56. A method for determining the stage of a biological condition in animal tissue comprising,
- collecting a sample comprising cells from the tissue,
- 30 determining an expression pattern of the cells as defined in any of claims 43-54,
- correlating the determined expression pattern to a reference pattern,
- determining the stage of the biological condition is said tissue.
- 35 57. A method for reducing cell tumorigenicity or malignancy of a cell, said method comprising

contacting a tumor cell with at least one peptide expressed by at least one gene selected from the group of genes consisting of gene Nos. 200-214, 233, 234, 235, 236, 244, 249, 251, 252, 255, 256, 259, 261, 262, 266, 268, 269, 273, 274, 275, 276, 277, 279, 280, 281, 282, 285, 286, 289, 293, 295, 296, 299, 301, 304, 306, 307, 308, 311, 312, 313, 314, 320, 322, 323, 325, 326, 327, 328, 330, 331, 332, 333, 334, 338, 341, 342, 343, 345, 348, 349, 350, 351, 352, 353, 355, 357, 360, 361, 363, 366, 367, 370, 373, 374, 375, 376, 385, 386, 387, 389, 390, 392, 394, 398, 400, 401, 405, 406, 407, 408, 410, 411, 412, 414, 415, 416, 418, 424, 426, 428, 433, 434, 435, 436, 438, 439, 440, 441, 442, 443, 445, 446, 453, 460, 461, 463, 464, 465, 466, 467, 469, 470, 471, 472, 473, 475, 476, 477, 479, 480, 481, 482, 483, 485, 486, 487, 488, 490, 492, 494, 496, 497, 498, 499, 503, 515, 516, 517, 521, 526, 527, 528, 530, 532, 533, 537, 539, 540, 541, 542, 543, 545, 554, 557, 560,

58. The method according to claim 57, wherein the tumor cell is contacted with at least two different peptides.

15

59. A method for reducing cell tumorigenicity of a cell, said method comprising

obtaining at least one gene selected from the group of genes consisting of gene No. 200-214, 233, 234, 235, 236, 244, 249, 251, 252, 255, 256, 259, 261, 262, 266, 268, 269, 273, 274, 275, 276, 277, 279, 280, 281, 282, 285, 286, 289, 293, 295, 296, 299, 301, 304, 306, 307, 308, 311, 312, 313, 314, 320, 322, 323, 325, 326, 327, 328, 330, 331, 332, 333, 334, 338, 341, 342, 343, 345, 348, 349, 350, 351, 352, 353, 355, 357, 360, 361, 363, 366, 367, 370, 373, 374, 375, 376, 385, 386, 387, 389, 390, 392, 394, 398, 400, 401, 405, 406, 407, 408, 410, 411, 412, 414, 415, 416, 418, 424, 426, 428, 433, 434, 435, 436, 438, 439, 440, 441, 442, 443, 445, 446, 453, 460, 461, 463, 464, 465, 466, 467, 469, 470, 471, 472, 473, 475, 476, 477, 479, 480, 481, 482, 483, 485, 486, 487, 488, 490, 492, 494, 496, 497, 498, 499, 503, 515, 516, 517, 521, 526, 527, 528, 530, 532, 533, 537, 539, 540, 541, 542, 543, 545, 554, 557, 560,

30 introducing said at least one gene into the tumor cell in a manner allowing expression of said gene(s).

60. The method according to claim 59, wherein at least one gene is introduced into the tumor cell.

35

61. The method according to claim 59 or 60, wherein at least two different genes are introduced into the tumor cell.

62. A method for reducing cell tumorigenicity or malignancy of a cell, said method comprising

5 obtaining at least one nucleotide probe capable of hybridising with at least one gene of a tumor cell, said at least one gene being selected from the group of genes consisting of gene Nos. 1-199, 215-232, 237, 238, 239, 240, 241, 242, 243, 245, 246, 247, 248, 250, 253, 254, 257, 258, 260, 263, 264, 265, 267, 270, 271, 272, 278, 283, 284, 287, 288, 290, 291, 292, 294, 297, 298, 300, 302, 303, 305, 309, 310, 315, 316, 317, 318, 319, 321, 324, 329, 335, 336, 337, 339, 340, 344, 346, 347, 354, 356, 358, 359, 362, 10 364, 365, 368, 369, 371, 372, 377, 378, 379, 380, 381, 382, 383, 384, 388, 391, 393, 395, 396, 397, 399, 402, 403, 404, 409, 413, 417, 419, 420, 421, 422, 423, 425, 427, 429, 430, 431, 432, 437, 444, 447, 448, 449, 450, 451, 452, 454, 455, 456, 457, 458, 459, 462, 468, 474, 478, 484, 489, 491, 493, 495, 500, 501, 502, 504, 505, 506, 507, 508, 509, 510, 511, 512, 513, 514, 518, 519, 520, 522, 523, 524, 525, 529, 531, 534, 15 535, 536, 538, 544, 546, 547, 548, 549, 550, 551, 552, 553, 555, 556, 558, 559, 561, 562,

introducing said at least one nucleotide probe into the tumor cell in a manner allowing the probe to hybridise to the at least one gene, thereby inhibiting expression of said at 20 least one gene.

63. The method according to claim 62, wherein at least one gene is introduced into the tumor cell.

25 64. The method according to claim 62 or 63, wherein at least two different genes are introduced into the tumor cell.

65. A pharmaceutical composition for the treatment of a biological condition comprising at least one antibody against an expression product of a cell from a biological tissue 30 produced by

obtaining expression product(s) from at least one gene said gene being selected from the group of genes consisting of genes as defined in claim 62,

35 immunising a mammal with said expression product(s) obtaining antibodies against the expression product.

66. A pharmaceutical composition for the treatment of a biological condition comprising at least one peptide, said peptide being an expression product from a gene selected from the group consisting of genes Nos. 1-562 of or a fragment thereof.
- 5 67. A vaccine for the prophylaxis or treatment of a biological condition comprising at least one expression product from at least one gene said gene being selected from the group of genes consisting of gene as defined in claim 62.
- 10 68. Use of a method as defined in any of claims 1-64 for producing an assay for diagnosing a biological condition in animal tissue.
69. Use of a at least one expression product from at least one gene for preparation of a pharmaceutical composition for the treatment of a biological condition in animal tissue.
- 15 70. Use of a gene, said gene being selected from the group of genes consisting of gene No. 1 to gene No. 562, for the preparation of a pharmaceutical composition for the treatment of a biological condition in animal tissue.
- 20 71. Use of a probe as defined in any of claims 62-64 for the preparation of a pharmaceutical composition for the treatment of a biological condition in animal tissue.
72. An assay for predicting the prognosis of a biological condition in animal tissue, comprising
- 25 at least one first marker capable of detecting an expression level of at least one gene selected from the group of genes consisting of gene No. 1 to gene No. 562.
73. The assay according to claim 72, wherein the marker is a nucleotide probe.
- 30 74. The assay according to claim 72, wherein the marker is an antibody.
75. The assay according to claim 72, comprising at least a first marker and/or a second marker, wherein the first marker is capable of detecting a gene from a first gene group as defined in claim 34, and/or the second marker is capable of detecting a gene from a
- 35 second gene group as defined in claim 34.
76. The assay according to any of claims 72-75, said assay further comprising means for correlating the expression level of the at least one gene to a standard expression level and/or a reference expression pattern.